

### Remarks

This paper is supplemental to the second preliminary amendment filed December 15, 2004 and assumes entry of the amendment contained therein.

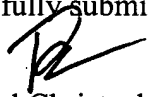
The Applicants have amended several of the claims to place them into better condition for examination on the merits. For example, Claim 1 has been amended to recite a pharmaceutical composition active on angiogenesis comprising the active agent. Support may be found in paragraph [0013] and elsewhere. Further editorial amendments have also been made to Claim 1. Similarly, Claims 3 and 4 have been amended for editorial purposes in view of the amendments to Claim 1.

The dependencies of Claims 5 and 6 have been changed from Claim 1 to Claim 4. Also, Claims 7 and 12 have been amended into independent form. Claim 18 has been amended to correct a minor typographical error.

Claims 26 and 27 are new claims that have been added and depend from Claim 1. Claim 26 recites that the molecule which inhibits expression of a nucleic acid molecule of a gene coding for protein IRS-1 is the nucleotide sequence SEQ ID NO. 3 or a fragment thereof comprising at least 12 contiguous nucleotides or derivatives thereof. Similarly, Claim 27 is substantially the same as Claim 26 except that it recites SEQ ID NO. 4 instead of SEQ ID NO. 3. Support may be found in paragraph [0016], for example, and elsewhere.

Entry of the above changes and the two new claims into the Official File is respectfully requested. Examination on the merits is respectfully requested.

Respectfully submitted,



T. Daniel Christenbury  
Reg. No. 31,750  
Attorney for Applicant

TDC:lh  
(215) 656-3381